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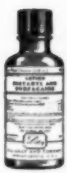

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CONTENTS

EDITORIAL

RECRUITING STUDENTS FOR PHARMACY

THE pharmacist is largely the product of the training he has received but this in turn is controlled to a large degree by the quality of the pharmacy student entering college. Try as they may our colleges can never turn out scientifically competent, professionally minded and socially conscious graduates if they take as raw material boys and girls who are weak in mathematics and science, have little motivation toward the profession, and have a social background above which they can hardly be expected to rise.

Over the past few years the number of young people becoming of college age has been much less. This is a reflection of the lowered birth rate which took place during the early thirties, the depression years. As a result, all fields of study have been competing for the student supply. Some have devised very ingenious plans for interesting bright, capable students in their areas of training.

More than any other single factor, however, are the activities and the attitudes of those who are already engaged in a given business or profession. The public almost invariably reflects the opinion of the practitioner concerning the merits and demerits of his chosen career. Not only are his statements concerning his happiness or unhappiness, success or failure given full consideration but also the obvious things in his environment, his dress, and activities are carefully surveyed. It is, therefore, small wonder that the physician who is respected, prosperous and seemingly quite happy in his work leads many young men with great intellectual capacity to seek a medical education in spite of the fact that it requires at least ten years for its completion, is hard and very costly. Another prime factor is that one rarely hears a physician bemoan his fate and decry those who would enter the profession, and yet medicine properly practiced is a hard life and one requiring great personal sacrifice. A physician's time is never his own. Emergencies arise at all hours, and an interrupted night's sleep is the rule rather than the exception. Even our vital statistics show that life-expectancy for physicians is less than that for their patients

of the same age. Still the public views the medical profession as one of the best fields of human endeavor.

Pharmacy, too, has its strength and weakness, its advantages and disadvantages. The monetary reward of the pharmacist on the average is stated to exceed that of both the dentist and the lawyer. Working hours, today, are fairly reasonable and working conditions pleasant. The pharmacist has great opportunity for self-employment with all the independence of thought and action that this brings. He is respected in his community and has an opportunity for public service unequalled except possibly by the physician. In spite of all these attributes of pharmacy many pharmacists disparage the profession and widely proclaim their dissatisfaction at having made such a poor choice of careers.

The psychological explanation of this is not at all clear. Some, undoubtedly, by some subconscious process of reasoning hope to cover up their real success and thus avoid competition. Many others view their state of affairs as does the typical farmer who is never satisfied with the weather in spite of bumper crops. Pharmacists are notorious for their poor psychology for is it not a common fault that they readily criticize their nearest competitior and thus succeed in lowering their prestige and that of the profession as well as his? Physicians are far too wise to make such an obvious blunder.

It is tragic to see bright young boys and girls whom the profession needs desperately told by their neighborhood pharmacist when they show an interest in pharmacy that they had better see a psychiatrist. It is the pharmacist here who needs psychiatric help. While it is admittedly unwise to try to coax and cajole young people to enter a field in which they have no real interest, it is wrong to list only the bad features to one who wishes guidance and information.

The pharmaceutical profession needs capable, high calibre recruits if it is to advance and develop as it should. Pharmacists in their neighborhood contacts should present pharmacy in its true light to those who seek advice. They should, furthermore, not dim the vision and the idealism of youth by deliberately subjecting them to the sordid and seamy side of the profession. Each profession has its full share of negative values but the profession endures and serves in spite of these not because of them or to glorify them.

L. F. Tice

A NOTE ON RAUWOLFIA SERPENTINA

By Heber W. Youngken, Sr.*

RAUWOLFIA, an old drug used in the empiric medicine of India for centuries as a purgative, anthelmintic and antidote for snake and insect bites and more recently in that country in clinical medicine as a hypotensive agent and as a sedative in the treatment of insomnia and certain forms of insanity, has recently been introduced into clinical medicine in the United States for use in the treatment of hypertension. Huge amounts have been imported from various districts of India and Malaya by manufacturing pharmaceutical firms and at least three products of this drug have lately appeared on the American market.

The drug represents the dried root of *Rauwolfia serpentina* Benth., a subshrub of the *Apocynaceae* native to India, Burma, Ceylon and Malaya and found growing in the Philippines and some other Asiatic countries. It is included in The Indian Pharmacopœia List (Calcutta 1946) which is published by the Department of Health of the Government of India. This work specifies that its bark is to be intact, that it be collected from 3 to 4 year plants in autumn, and that it contain not more than 2 per cent of other organic matter and not less than 0.8 percent of total alkaloids of Rauwolfia.

Chemical investigations of *Rauwolfia serpentina* root have revealed the presence therein of the following alkaloids: ajmaline, ajmalanine, ajmalicine, serpentine, serpentinine, and rauwolfine, also a resin, and other principles of lesser importance therapeutically.

The purpose of this note is to make a preliminary report of some of the author's findings which pertain to the identification of the authentic drug and distinguish it from its more common substitutes and adulterants which have been encountered in the examination of commercial lots labeled "Rauwolfia Serpentina Root".

Description of Rauwolfia Serpentina Root

The root of *Rauwolfia serpentina* Benth. is conical, tortuous and curved, of varying length and up to about 20 mm. in width at the summit; externally grayish-yellow to brown, sometimes with purplish blotches, as in the Bengal variety, slightly wrinkled to rough and irregularly longitudinally wrinkled in thicker and older parts.

* Massachusetts College of Pharmacy, Boston.
Received June 4, 1953.

The commercial drug usually occurs as cylindrical to cylindrical tapering segments from 2 to 20 cm. in length and from 5 mm. to 20 mm. in diameter. Its fracture is short, irregular, breaking in sufficiently long segments with a snap and exhibiting some projecting strands of cork along the periphery. Its fractured surface exhibits a grayish-yellow bark and a yellowish white to pale yellow wood, the latter of hard texture and occupying most of the diameter of the root. Its odor is indistinct, its taste, bitter.

FIG. 1—*Rauwolfia serpentina* Benth. (2/3 ×) Leaf and flowering branch, in center; to left above, an inflorescence; below, a cross segment of root.

Microscopical Examination

Rauwolfia serpentina roots of commerce exhibit the typical structure of a perennial dicotyl root of secondary growth, showing the following tissue regions from periphery to the center of the cross and radial longitudinal sections: cork, phellogen, secondary cortex, phloem, cambium, secondary xylem, and primary xylem.

The more important special characteristics whereby diagnosis of genuine *Rauwolfia serpentina* roots can be made are as follows:

The cork shows stratification which is sometimes not apparent in sections of thick older root segments owing to exfoliation. In this stratification one sees alternating strips of narrower and smaller and of radially broader and larger cork cells. There are from 2 to 6 or 7 of such strips. The strip of larger cork cells lying between two strips of narrower and smaller cork cells consists of from 1 to 5 layers of thin-walled, rectangular cork cells not of uniform radial width, those bordering on the strip of narrower cork cells being generally of smaller radial width than those lying in the middle of the zone.

The secondary cortex is composed of starch-bearing parenchyma, its cells being well filled with starch grains in sections which are not cleared. It is devoid of fibers and stone cells.

The phloem is also devoid of stone cells and fibers. The phloem ray cells are mostly elongated and contain starch grains up to about 14 μ in diameter. In some roots monoclinic prisms of calcium oxalate occur in this region.

The xylem consists of narrow, radially elongated wood wedges separated by xylem rays which vary in range of breadth in different ecological varieties of the root. Each wood wedge consists of pitted and occasional reticulate vessels, fibers, tracheids and wood parenchyma. The simple pitted type of vessel and tracheid predominates, and, where the walls of the vessels are in contact with the parenchyma of the xylem rays, bordered pits occur. The perforation rims occur both at the ends and on the side walls of the vessels. Vessels, tracheids and fibers possess lignified walls. The xylem rays are mostly 1 to 5 cells in width, less frequently from 1 to 8 cells in width. The ray cells contain starch and possess pitted walls. The vessels are averagely narrower lumened and relatively fewer in number than in the most frequently encountered adulterant and substitute root, *Rauwolfia*

canescens. Resin cells may occur in the cortex, phloem and xylem and are especially abundant in the Dehra Dun variety.

The starch grains are mos.ly single, spheroidal, muller-shaped to oval but occasionally are 2- to 3-compound, the individual unaltered grains mostly up to 19μ but occasionally up to 27μ, and the altered starch, up to 40μ in diameter.

The roots of several other species of *Rauwolfia* namely *R. canescens, R. perakensis* and *R. densiflora* have been found as substitutes and adulterants in the commercial drug. The most common of these has been the root of *R. canescens* which frequently occurs in areas of India where *R. surpentina* abounds. The more important diagnostic differences between the commercial roots of *Rauwolfia serpentina* and *R. canescens* are as follows:

Rauwolfia serpentina	*Rauwolfia canescens*
Cork in alternating zones of larger and smaller cork cells	Cork of a single zone of narrow more or less rectangular cells
Sclerenchyma elements absent in the secondary phloem and cortex	Sclerenchyma elements present in the secondary phloem
Xylem vessels smaller and less numerous in sections of similar diameter	Xylem vessels larger and more numerous in sections of similar diameter
Wood fibers up to about 700μ in length	Wood fibers up to about 1500μ in length

The root segments of *Rauwolfia perakensis* from Malaya and *R. densiflora* from India are harder in texture than those of the *R. serpentina* and *R. canescens* and possess a splintery fracture in sufficiently long pieces. Short segments are unbreakable by hand. Both possess sclerenchyma elements scattered in the secondary phloem and most of the stone cells are arranged singly. Both have stratified cork. Further studies of these roots are in progress and will be reported later.

Acknowledgment

Grateful acknowledgment is made to S. C. Datta of the Pharmacognosy Laboratory, Government of India, and to Riker Laboratories, Inc. for the authentic materials used in this study.

OCCURRENCE OF RUTIN IN PLANTS*

By C. F. Krewson and J. Naghski

RUTIN has been known for more than a century to be a constituent of plants. It was first discovered in 1842 by August Weiss, a Nuremburg apothecary, who obtained it from the leaves of the garden rue (*Ruta graveolens*), whence its name. Subsequently, Bornträger (5) studied this compound, and being misled by the ease with which it dissolved in alkaline solutions, believed it to be an acid and so termed it "rutinic acid". There was much confusion among the early investigators relative to the characterization of rutin. This was due mainly to the fact that rutin was not easy to purify, and its extremely hygroscopic nature made it difficult to obtain accurate analytical values for carbon and hydrogen. It was not until 1896 that the composition of the sugar moiety was established by Schmidt (68) and the correct empirical formula, $C_{27}H_{30}O_{16}$, assigned. The early history of rutin has been reviewed by Perkin and Everest (59) and by Charaux (12, 13).

Rutin and the related flavonols were formerly used as dyestuffs for textile fibers, but were displaced by the synthetic dyes. Today only small quantities of the flavonols quercetin and quercitrin (in the form of orange and lemon flavine) are utilized as pigments.

The use of rutin as a medicinal agent has greatly stimulated production of this compound. Demands for this drug have prompted many investigators not only to re-evaluate old sources but also to search for new ones.

Since much of the older literature on the occurrence of rutin in plants is widely scattered and not readily accessible, and since we have had a number of requests for information of this kind, we thought it advisable to make this literature survey.

Plants containing rutin: It was found that rutin is widely distributed in the plant kingdom. At present at least 32 plant families and 65 plant species are known that contain it. Thirty-one of these are tabulated in Table I in alphabetical order according to the family

* Eastern Regional Research Laboratory, Philadelphia 18, Pennsylvania, one of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, United States Department of Agriculture.

TABLE I

PLANTS CONTAINING RUTIN

Family	Genus and Species	References	Rutin Content, % *
APOCYNACEAE	*Nerium odorum* Lam.	53	—
BORRAGINACEAE	*Lithospermum officinale* Linn.	13	—
ARALIACEAE	*Hedera helix* Linn.	13	—
CAPPARIDACEAE	*Capparis spinosa* Linn. (Capers)	8, 13, 32, 63, 69, 92	0.32 (8)
CAPRIFOLIACEAE	*Sambucus canadensis* Linn. (Elder)	38, 66, 83	0.77, F (66); 3.5, L (83); 5.2, IF (83); 3.0, MF (83)
	Sambucus nigra Linn. (*S. vulgaris* Lam.) (Elder)	13, 44	—
CRASSULACEAE	*Bryophyllum calycinum* Salisb. (*B. pinnatum*, Kurg)	85	L
	Sedum acre Linn.	48	—
CRUCIFERAE	*Bunias orientalis*	37	—
EMPETRACEAE	*Empetrum nigrum* Linn. (Smokeberry, crowberry)	36	—
EUPHORBIACEAE	*Mallotus japonicus* Muell Arg.	75	—
GLOBULARIACEAE	*Globularia alypum* Linn.	82, 92	2.5, F (82)
	Globularia vulgaris Linn.	82, 92	—
HIPPOCASTANACEAE	*Aesculus californica* Nutt (Pavia C.)	13	—
LEGUMINOSAE	*Daviesia latifolia* R. Br. (Native hop-bush)	61	—
	Sophora japonica Linn. (Chinese scholar tree, Japanese pagoda tree)	19, 27, 47, 74, 78, 79, 81	3.0, F (81); 16.3-22.9, F (19)
	Tephrosia purpurea Pers. (Ash vetch)	14	2.5
LILIACEAE	*Asparagus officinalis* Linn.	11, 22, 52, 80	1.01, MP (80)
MAGNOLIACEAE	*Magnolia grandiflora* Linn.	60	—
	Magnolia kobus DC.	31	—
	Magnolia macrophylla Michx.	43	—
	Magnolia obovata Thumb	60	—
	Magnolia soulangeana Soul.	60	—
	Magnolia stellata Maxim	60	—
	Magnolia thompsoniana Hort.	60	—
	Magnolia umbrella Lamb.	43	—
	Magnolia yulan Desf.	60, 88	2.4, F (60)

* F = Flowers
L = Leaves
IF = Immature Flowers
MF = Mature Flowers
MP = Mature Plant

Family	Genus and Species	References	Rutin Content, % *
MYRTACEAE	*Eucalyptus macrorrhyncha* F. v. M.	41, 45, 58, 64, 70, 76, 77	10.0, L (77); 13.7-23.1, L (41); 6.0-24.0, L (64)
	Eucalyptus youmani B. and McK.	64	6.8-11.0, L
OLEACEAE	*Forsythia fortunei* Rehd.	51	2.08-4.29, F
	Forsythia pendulata Linn.	29	0.36, F
	Forsythia suspensa Vahl.	25, 51	1.09 F (51)
PALMAE	*Dactylifera palma* Linn. (Date palm)	24	0.36, PG
PAPAVERACEAE	*Eschscholtzia californica* Cham.	65	5.0, F
	Hypecoum pendulum Linn.	13	——
PAPILIONATAE	*Onobrychis sativa* Lam.	4	0.3-0.4, P
POLYGONACEAE	*Fagopyrum cymosum*	35	4.0 (May) 8.5 (Oct)
	Fagopyrum emarginatum	20	——
	Fagopyrum esculentum Mnch. (*Polygonum fagopyrum* Linn.) (Japanese buckwheat)	7, 18, 71, 72, 73, 91	0.11, L (72); 1.78, L (91); 0.71, F (91); 2.0+, F (91); 1.16-6.37, L, F (18)
	Fagopyrum tataricum (Gaertn. (Tartary buckwheat)	20	3.4-5.0, P
	Fagopyrum tetra-tataricum S.	20	——
	Muehlenbeckia chilensis Meissn.	33, 34	2.4, P (33)
PROTEACEAE	*Grevillea robusta* Cunn.	39	0.52, L
RHAMNACEAE	*Paliurus aculeatus* Lam. (*Rhamnus paliurus* Linn.)	57	0.15, GF
ROSACEAE	*Prunus melanocarpa* (A. Nels) Rydb. (Wild cherry)	15	1.44-3.88, L
RUBIACEAE	*Galium cruciatum* Linn.	13	——
RUTACEAE	*Citrus hybrid*	40	0.9-3.2, PE
	Ruta graveolens Linn. (Garden rue)	5, 26, 32, 69, 87	2.0, P (26)
SALICACEAE	*Salix triandra* Linn. (*S. amygdalina*, β-*triandra* L.)	9	0.15-0.70
SANTALACEAE	*Osyris abyssinica* Hochst.	1	——
	Osyris compressa DC. (Cape sumach)	57, 58	——
SAXIFRAGACEAE	*Hydrangea paniculata* (Grandiflora Sieb)	17	4.1, F

* F = Flowers P = Plants
L = Leaves PE = Peel
GF = Green Fruit PG = Pollen Grains

Family	Genus and Species	References	Rutin Content, % *
SOLANACEAE	*Lycopersicum pimpinellifolium* (Red Currant Tomato)	28	0.037, L
	Nicotiana glauca	2, 13, 23	1.2-2.1, L (2)
	Nicotiana rustica Linn.	2	0.1-0.7, L (2)
	Nicotiana tabacum Linn.	16, 23, 30, 54, 55, 56	0.008-0.61; ave. 0.40, L (16)
	Solanum angustifolium R. and Pav.	84	0.75, P
	Solanum demissum Lindle	67	——
	Solanum lycopersicum Linn. (L. esculentum Mill.) (tomato)	3	——
	Solanum tuberosum Linn. (potato)	13	——
UMBELLIFERAE	*Bupleurum falcatum* Linn.	62	0.3-0.4, P
	Heracleum spondylium Linn.	13	——
VIOLACEAE	*Viola lutea splendens*	50	16.6, F
	Viola tricolor Linn. (Arvensis and vulgaris)	21, 46, 58, 70, 90	0.13, L; 0.08, S; 0.05, R (70); 2.0 (90)
	Viola tricolor Linn. Var. Maxima (Giant Roggli)	50	18.3-21.2, F
	Viola tricolor Linn. (Odorata)	6	——

* F = Flowers R = Roots
L = Leaves S = Stems
P = Plants

name. References are given to the original investigators and to others who have contributed to the identification of rutin. When available, the percentage rutin content is also given.

In addition to the spermatophytes listed in Table I, rutin has also been isolated from a thallophyte. Kuhn and Low (42) isolated it from the gametes of a *Chlamydomonas* mutant, which they termed *Chlamydomonas agametos.*

In the quest for new sources of rutin, there will undoubtedly be much duplication of effort, since since negative findings are not usually reported. In a search for steroidal saponins, Wall et al. (86) are extending the screening of plant extracts to include other constituents, among which are flavonoids. Of approximately 1,000 plant samples from 29 families, listed in their initial report (86), about two-thirds of which were of the genera Agave, Yucca, and Dioscorea, most were devoid of flavonoids. But 33 samples are listed that contain flavonoids in trace amounts and 4 in moderate quantities. The test used in this work was the cyanidin reaction of Willstätter (89, 10) which, although not specific for rutin, indicates the presence of flavonoids.

Plants containing no appreciable rutin: During a routine examination at the Eastern Regional Research Laboratory, many domestic plants, the extracts of which gave a positive cyanidin test failed to yield rutin by the gravimetric technique of Naghski et al. (49), based on the isolation of the flavonoid. This method, however, is not sensitive to small quantities of rutin (less than 0.1%), and so plants containing only traces would escape detection. Plants in which no rutin was found by the gravimetric analysis are listed in Table II:

TABLE II

PLANTS CONTAINING NO APPRECIABLE RUTIN

Family	Genus and Species	Part Examined
ANACARDIACEAE	*Rhus* glabra Linn. (sumac)	Fresh flowering heads
BALSAMINACEAE	*Impatiens pallida* Nutt. (Jewelweed)	Fresh whole plant
BERBERIDACEAE	*Podophyllum peltatum* Linn. (May-apple)	Fresh whole plant
BORAGINACEAE	*Borago officinalis* Linn. (Borage)	Fresh leaves
CANNABINOIDEAE	*Humulus lupulus* Linn. (Hop)	Dried flowers
CAPRIFOLIACEAE	*Viburnum opulus* Linn. (Snowball)	Fresh flowers
CARYOPHYLLIACEAE	*Stellaria media* Vill. (Chickweed)	Fresh whole plant
CHENOPODIACEAE	*Beta vulgaris* Linn. (Beet)	Fresh tops
	Var. cicla (Swiss chard)	Fresh leaves
	Spinacea oleracea Linn. (Spinach)	Fresh leaf
	Spiraea vanhouttei Zabel (Spirea, Bridal wreath)	Fresh flowers
COMPOSITAE	*Aster novae-angliae* Linn. (New England aster)	Fresh flowers
	Cichorium intybus Linn. (Chicory)	Fresh white flowers
	Chrysanthemum carinatum Schousb.	Fresh yellow flowers
	Chrysanthemum parthenium Pers. (Feverfew)	Fresh flowers
	Galinsoga ciliata (Raf.) Blake	Whole plant
	Lactuca sativa Linn. (Lettuce)	Fresh leaf
CONVOLVULACEAE	*Ipomoea batatas* Poir. (Sweet potato)	Fresh vines
CRUCIFERAE	*Brassica arvensis* Kuntze (Mustard weed)	Fresh yellow flowers
	Brassica oleracea Linn. (Var. *acephala*, Kale; var. *Botrytis* Linn., Broccoli; var. *capitata alba* Linn., Cabbage)	Fresh flowering heads and attached leaflets
CUCURBITACEAE	*Cucurbita pepo* Linn. (Pumpkin)	Fresh ripe rind; Fresh blossoms
EQUISETACEAE	*Equisetum hiemale* Linn. (Horsetail or Scouring-rush)	Fresh whole plant
EUPHORBIACEAE	*Euphorbia epithymoides* Jacq. (E. polychroma Kern.) (Spurge)	Fresh whole plant
GNETACEAE	*Ephedra viridis* Wats. (Mexican-tea)	Dried whole plant
GRAMINEAE	*Holcus sorghum* Linn. (var. White Hegari)	Fresh whole plant
	Lolium perenne Linn. (Ryegrass)	Fresh whole plant
	Setaria glauca Beauv. (Yellow foxtail)	Fresh whole plant
IRIDACEAE	*Iris pseudacorus* Linn. (var. Seminole-Yellow flag)	Fresh flowers

Family	Genus and Species	Part Examined
LABIATAE	*Coleus sp.*	Fresh plant
	Mentha spicata Huds. (Spearmint)	Fresh leaf
LEGUMINOSAE	*Medicago sativa* Linn. (Alfalfa)	Fresh whole plant
	Glycine soja Sieb. and Zucc. (*Phascolus max* Linn.) (Soybean)	Fresh leaf, less most of stem
	Trifolium repens Linn. (White clover)	Fresh blossoms
LILIACEAE	*Convallaria majalis* Linn. (Lily-of-the Valley)	Fresh leaves and blossoms
MALVACEAE	*Althaea rosea* Cav. (Hollyhock)	Fresh flowers
	Gossypium hirsutum Linn. (Cotton)	Dried leaves
	Malva rotundifolia Linn. (Common mallow)	Fresh whole plant
MORACEAE	*Broussonetia papyrifera* Vent. (Paper-mulberry)	Fresh flowers
MYRTACEAE	*Eucalyptus baueriana* Schau.	Dried leaves
	E. botryoides Sm.	Dried leaves
	E. cornuta Labill.	Dried leaves
	E. corynocalyx F. v. M.	Dried leaves
	E. costata Br. aff.	Dried leaves
	E. crebra F. v. M.	Dried leaves
	E. eugenioides Sieb.	Dried leaves
	E. ficifolia F. v. M.	Dried leaves
	E. globulus Labill.	Dried leaves
	E. goniocalyx F. v. M.	Dried leaves
	E. leucoxylon F. v. M.	Dried leaves
	E. paniculata Sm.	Dried leaves
	E. polyanthemos Schau.	Dried leaves
	E. robusta Sm.	Dried leaves
	E. rostrata Schl.	Dried leaves
	E. rudis Endl.	Dried leaves
	E. salmonophloia F. v. M.	Dried leaves
	E. sideroxylon Cunn.	Dried leaves
	E. tereticornis Sm.	Dried leaves
	E. viminalis Labill.	Dried leaves
PHYTOLACCACEAE	*Phytolacca decandra* Linn. (Pokeweed)	Fresh leaves
POLYGONACEAE	*Eriogonum giganteum*	Dried whole flowers
	Fagopyrum esculentum Linn.	Buckwheat seed and honey
	Polygonum persicaria Linn. (Smartweed, Ladysthumb)	Fresh whole plants
	Rheum rhapanticum Linn. (Rhubarb, Pieplant)	Fresh leaf
	Rumex crispus Linn. (Yellow dock)	Fresh plant
	Rumex hymenosepalus Torr. (Canaigre)	Dried root

Family	Genus and Species	Part Examined
PORTULACACEAE	*Portulaca oleracea* Linn. (Pusley)	Fresh whole plant
RANUNCULACEAE	*Paeonia sp.* (White peony)	Fresh flowers
	Ranunculus bulbosus Linn. (Common field buttercup)	Fresh flowers
ROSACEAE	*Prunus serotina* Ehrh. (Wild black cherry)	Dried leaves
RUTACEAE	*Citrus aurantifolia* Swingle (*Limonia aurantifolia* Ch.) (Lime)	Fresh immature peel and fruit
	Citrus grandis Osbeck (*Citrus decumana* Linn.) (Grapefruit)	Fresh mature peel and fruit
	Citrus limonia Osbeck (Lemon)	Fresh immature peel and fruit
	Citrus sinensis Osbeck (Common orange)	Fresh mature peel and fruit
SAXIFRAGACEAE	*Hydrangea arborescens* Linn.	Flowering heads and stipules only in early bud
	Philadelphus coronarius Linn. (Mock-orange)	Fresh blossoms
SOLANCEAE	*Capsicum annum* Linn. (Pepper)	Fresh immature fruit
	Lycopersicon esculentum Mill. (*Solanum lycopersicum* Linn.) Var. Stone (Tomato)	Vine and fruit (green and ripe)
UMBELLIFERAE	*Daucus carota* Linn., Var. sativa (Wild Queen-Anneslace)	Flower head
	Petroselinum hortense Hoffm. (Parsley)	Fresh leaf
URTICACEAE	*Raminum nivcum* Linn. (Ramie)	Fresh tops and leaves
VIOLACEAE	*Viola papilionacea* Pursh. (Common violet)	Fresh white flowers

Summary

A survey was made of literature on the occurrence of rutin in plants. Rutin has now been reported present in at least 32 plant families, representing at least 65 plant species. Examination of 80 species representing 21 additional families failed to show any rutin.

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RUM RESEARCH IN THE COMMONWEALTH OF PUERTO RICO

By T. Swann Harding *

DURING March 1953 the University of Puerto Rico celebrated its fiftieth anniversary with considerable éclat. On the 18th of the month the Rum Pilot Plant, Agricultural Experiment Station, University of Puerto Rico, was dedicated. The Station which has been directed since 1943 by Dr. Don Arturo Roque, is a division of the University headed by Chancellor Jaime Benítez, and Victor Rodríguez Benítez is Technical Director of the Rum Pilot Plant.

The Plant was built and equipped at a cost in the neighborhood of four hundred thousand dollars and is thoroughly modern in both architecture and facilities. It contains the latest in laboratories and offices, the very best modern machinery, and an experimental still with a production capacity of approximately 150 proof-gallons daily. It is designed to study all aspects of the manufacture of rum and alcohol. As the accompanying illustrations show, both the external structure and at least the female technical staff are singularly beautiful.

Puerto Rico depends for its economic well-being essentially on the income derived from the sugar industry. Many of the mills operate at a low margin of profit, hence disposal of the end-product, black-strap molasses, must be had at a reasonable price. One of its most important and profitable uses is for the making of rum. During the fiscal years 1941-42 to 1946-47 the Island derived from rum taxes approximately $215,000,000.

This money was all used wisely. During a 4-year period such allocations as follows were made: For education $90,000,000; for health services and hospital construction $50,000,000; for industrial improvement $40,000,000; for the development of hydroelectric power $25,000,000; for various governmental agricultural agencies and activities $18,000,000; for road-building $15,000,000; for aqueduct expansion $8,000,000; and for advancement of the coffee industry $5,000,000. Other smaller sums went for public works and social

* English Technical Editor, Agricultural Experiment Station, University of Puerto Rico, Rio Piedras, P. R.

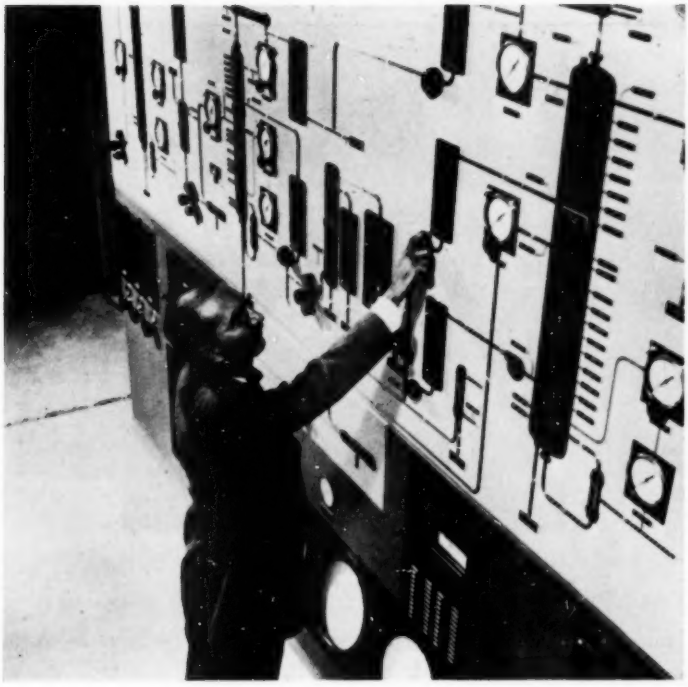
Rum Pilot Plant,
Agricultural Experiment Station,
University of Puerto Rico

and health services in wide variety. This income is obviously of great importance to the Puerto Rican Government.

During World War II and immediately after Puerto Rican rum first found a greatly enlarged market as it replaced unavailable whisky and other alcoholic drinks more commonly consumed in the United States. When whisky became available after the war, the U. S. market for Puerto Rican rum was reduced again.

Whereas, for instance, only about a million proof-gallons of Puerto Rican rum were shipped to the U. S. market in 1940, the figure rose to nearly two million the following year, to over three million in 1942, and to an all-time high of 9,529,973 proof-gallons in 1944. Shipments were less than half that in 1945, they had declined to 2,184,207 proof-gallons by 1947, and dropped precipitously to 397,795 proof-gallons in 1948.

Whereas also, the total rum revenues received by the Puerto Rican Government rose from $7,405,122 in 1941 to $71,449,228 in 1944, and were maintained above the forty-million-dollar figure in 1945-46, they dropped to $10,483,684 in 1948. The rise and fall of rum resulted from the two factors above-mentioned: The replace-



Technical Director Victor Rodríguez-Benítez
of the Rum Pilot Plant

ment of other distilled liquors with rum on the U. S. market during the war, and the combined ability once more to procure the customary liquors in the U. S. after the war.

In consequence of this situation Chancellor Jaime Benítez in 1945 requested Director Arturo Roque to undertake a program of rum research designed to establish standards of aging, identity, and quality for Puerto Rican rums. Governor Luis Muñoz-Marín also appointed a Rum Advisory Committee, and a long-range promotional program was undertaken for Puerto Rican rums. Some of the results of this are visible in the large advertisements that have appeared in many American magazines during the past 6 months.

The rum research immediately undertaken by the Agricultural Experiment Station dealt with rum-quality appraisal. As a result,

Technical Staff
Rum Pilot Plant

chemical methods were developed which are quite as good as classical panel testing for determining rum quality.

Rum is essentially a solution of 43 percent by volume of ethyl alcohol in water, and it contains only about 0.3 percent of impurities or congeners which give it its characteristic flavor and aroma. Some of these are desirable and some undesirable. They consist mostly of a mixture of 10 to 14 acids, 8 to 10 aldehydes, 5 to 7 higher alcohols, and over 20 different esters, with small quantities of acetals, essential oils, and tannins. Some rum processors also add such substances as sugars, caramel, wine, fruit extract, bark extract, root extract, and flavoring ingredients.

It would obviousiy be impossible to isolate each component and determine its bearing on quality. For this reason panel testing by a group of 10 experts was commonly resorted to; but the method is laborious, expensive, and somewhat unreliable. While the opinion of a group of tasters is usually reproducible, even the most expert individual tasters are often erratic. So work was undertaken to develop a simple, less expensive, but reliable, accurate, and reproducible chemical method of appraisal using over 200 samples of about 50 different rums.

The more beautiful contingent
Technical Staff, Rum Pilot Plant

The results were gratifying. The methods were based on electrometric titration curves of rum acids and esters. When plotted, the curves reflect differences in the quality and age of rums. Seven key points were established on the curves to characterize them. Combinations of the ordinates and abscissas of these seven points finally gave a series of over a hundred factors having the possibility of measuring rum quality. The analytical data were correlated with that secured from test panels and the method was found to be a reliable measure for the prediction of consumer acceptance.

Development of this quality-appraisal method has been of great value to the industry. It places manufacturing control on a scientific basis for the first time and serves also as a reliable guide for blending. An incidental finding was that during 1947, the public was buying the better rums in much greater quantity than the poorer ones. Since that time, as judged by the chemical-appraisal method, the rums of Puerto Rico have improved notably in quality. These quality-control methods are applied specifically to all rum intended for export, it being reasoned that competition in the local market in Puerto Rico will take care of quality control there automatically.

The research studies carried out so far at the plant have indicated that many factors hitherto regarded as important in rum-quality appraisal are really without significance. Among these were total congeners, total aldehydes, higher alcohols, esters or acids present, the index of refraction, total solids, viscosity, and color. The substances that impart flavor and aroma to rums are the same as those that do so to whiskies, insofar as natural flavoring ingredients are concerned. It is not the quantities present, however, so much as the nature of these substances that determines rum quality.

The optimum sugar content of a rum as related to consumer acceptance is under study. It has been found that continental U. S. tasters definitely prefer dry rums. In Puerto Rico, however, there is as definite a preference for somewhat sweeter rums. Rums manufactured for export, therefore, contain less sugar than those manufactured even for the local market.

Color standards that should be adopted for gold and white label rums are also under investigation. Suitable recommendations will be made later. For determining degree-proof the use of ebulliometers and hydrometers has been found to be less accurate than the determination of the specific gravity or the index of refraction on the distilled sample.

Much of the work just described had been performed and had had a favorable impact on the industry before the Rum Pilot Plant was proposed and built. The Legislature acted favorably on this proposal and construction of the building was completed by July 1951. Procuring the requisite personnel and equipment took a year or so longer. Then the laboratory-scale investigations being conducted in the Station's Department of Chemistry were transferred to the Rum Pilot Plant.

Some of the technical subjects now under study or which are to be studied in this unique institution which will pioneer in a field of research previously left largely to rule-of-thumb, are as follows:

1. A varietal study of pure-culture yeasts and the production of new strains by induced mutations and artificial hybridization to select those that produce the most acceptable flavor and aroma in rums, produce high yields, and have high fermentation efficiency.

2. Determination of the effects of molasses pretreatment on the quality and yield of rum produced.

3. A study of different methods of conducting fermentation and of the factors affecting yield and fermentation efficiency, such as sugar

concentration, yeast nutrients, temperature, pH, fermentation time, type of yeast strain, ratio of fermenting mash volume to internal fermenter surface, and degree of aeration and agitation.

4. A comparison of present-day batch-fermentation processes and the newer continuous fermentation processes.

5. A comparison of batch and continuous distillation processes as to their effects on rum quality.

6. The operation of distillation columns under pressure or under vacuum, at different alcoholic strengths of the distillates, and by extractive distillation, which should throw light on the effect of these on rum quality.

7. The influence of different factors on the rate of quality improvement in rums while aging, some significant variables being time, temperature, humidity, type and size of container, types of rum, degree-proof of the rum, and pretreatments of the rum in processing.

8. Studies of accelerated aging procedures, blending techniques, methods of conducting organoleptic tests, control methods for distillery and rectifying-plant operations, and analytical chemical methods for rum-quality appraisal, in additional aspects.

9. The profitable utilization of distillery byproducts and a study of processes for preparing liquers, gins, eau de cologne, rubbing alcohols, perfumes, antifreeze, ethyl acetate solvent, ethyl citrate, ethyl lactate, and ethyl itaconate.

All information obtained will be made freely available to the rum industry which cooperates with the Plant whole-heartedly. No effort will be made to dictate to the industry or to encourage the legislative establishment of complicated control measures. It is felt that the Immature Spirits Act, Law 354, approved March 25, 1949, as it stands, is a good guarantee to consumers of Puerto Rican rum that they will be supplied with a product of high quality. The broad aim of the research program will be to assist rum manufacturers in solving their technical problems.

More than half the Puerto Rican rum manufacturers have sent samples of their products to the Plant for analysis and have consulted it on technical phases of their work. The results and information developed at the Plant are made freely available to them. Its service includes the supplying of yeast cultures to be used in rum fermentation, free of charge. Inferior rum brands have already been banished

from the market and significant improvement has been obtained in the leading brands shipped out.

In 1951, rum shipments to the United States had risen to nearly two million proof-gallons. Rum revenues were then $21,486,926. It is felt that research conducted at the Agricultural Experiment Station and the Rum Pilot Plant played an important part in this improvement. Progress is regarded as sound and no longer based on a mere scarcity of whisky in the United States.

The Rum Pilot Plant is unique in conception and in research program. It is an admirable adjunct to the basic economy of the Island, and to the research facilities of the Agricultural Experiment Station.

IN VIVO EXPERIMENTS ON THE CARCINOGENICITY OF SEX AND PITUITARY HORMONES

By John R. Sampey, Ph.D.*

HORMONES are among the most widely used agents in the palliative treatment of neoplasms. A recent review of Nathanson and Kelley (44) evaluates the extensive literature on the subject.

Increasing attention is being given to the carcinogenic action of hormones. The present paper brings together some fifty articles which have appeared within the last four years on the carcinogenicity of the sex and pituitary hormones.

Estrogens

Diethylstilbestrol. The carcinogenic action of diethylstilbestrol has been investigated more thoroughly during the last four years than that of any other estrogen. Dunning and associates (11, 12) found that a high fat diet accelerated the growth of mammary tumors induced by this estrogen in rats, but that it did not increase the total number of malignant growths. Two years later these investigators published three additional studies (13, 14, 15) on the production of mammary tumors in various strains of rats by implants of diethylstilbestrol. King and coworkers (27) caused 100% incidence of mammary cancer in ovariectomized mice by feeding diethylstilbestrol.

Howard, McClure and Campbell have filed three interesting reports within the last four years on mammary and prostatic carcinoma in male patients after prolonged diethylstilbestrol therapy. Howard and Grosjean (23) described a bilateral mammary carcinoma in a male following lengthy treatment for carcinoma of prostate. McClure and Higgins (37) observed a similar phenomenon in a male patient with carcinoma of the bladder who was given the estrogen orally and who received estradiol dipropionate intramuscularly. Campbell and Cummins (6) reported that diethylstilbestrol caused a carcinoma of the prostate in one patient.

* Professor of Chemistry, Furman University, Greenville, S. C.

Kirkman (28, 30) has produced renal adenomas and carcinomas in hamsters by subcutaneous implants of diethylstilbestrol. Bacon (2) reported tumors of the epididymis and the uterus in hamsters by similar treatment. Intramuscular injections of this estrogen into R. I. L. strain of mice resulted in increased leukemia (43). When given orally to spayed guinea pigs it produced fibroid formation in the castration stump, abdominal and thoracic cavities (45). Ovarian cysts in rats were increased by subcutaneous injections of diethylstilbestrol (25). Liver tumors resulted when the estrogen was applied to the skin of mice or injected intraperitoneally (3).

Stilbestrol. Jakobsen (24) and Corbett and Adams (7) have reported that stilbestrol, like diethylstilbestrol, produced bilateral carcinoma of the breast in a male patient treated for carcinoma of the prostate. Stilbestrol pellets have induced testicular interstitial-cell tumors in mice (5), while Horning (22) produced malignant tumors in prostatic grafts with this estrogen.

Estradiol. Kirkman (30) showed that estradiol caused renal tumors in hamsters when injected subcutaneously. Long continued treatment with this estrogen or estradiol dipropionate resulted in fibromas in the vasa deferentia of rabbits (4). The benzoate of estradiol was more effective than the natural hormone in producing hypophysary adenomas in rats (16). The dipropionate given subcutaneously caused adrenal cortex adenomas in ovariectomized mice (17). The dipropionate, combined with x-rays, showed synergistic action in inducing thymic lymphosarcoma in mice (33).

Other Estrogens. The synthetic estrogen, dioxydiethylstilbene, caused adenomata in hypophysis of rats (49). Tri-p-anisylchloroethylene produced testicular interstitial cell tumors in mice (21). Lactogenic hormone stimulated the growth of a transplanted tumor in rats (18). X-rays and estrogens given simultaneously showed a synergistic action in inducing thymic lymphosarcoma in mice (32).

Dmochowski and Orr (8, 9, 10) published three papers in 1949 on the induction of breast tumors in mice with oestrone and methylcholanthrene. Others have reported mammary cancers induced in mice by the administration of estrogens (26, 47, 50). Kirkman and Bacon (29) studied kidney tumors in hamsters following estrogen treatment. Both estrogens and androgens induced uterine and cervical carcinomas in hybrid mice (19). Estrogen pellets induced leukemia in mice (34). Progesterone induced adenoma-like structures in rats when given orally or subcutaneously (36).

Androgens

Androsterone produced adenoma-like structures in rats when administered orally or subcutaneously (36). Spontaneous hepatomas in mice were increased by testosterone injections (1). Horning (22) produced tumors on prostatic grafts with testosterone. Sublingual administration of methyltestosterone to a patient resulted in a malignant tumor developing in the right lower quadrant (46). Bacon (2) noted the formation of tumors of the uterus of hamsters following subcutaneous administration of testosterone propionate, and Gardner (20) recorded ovarian and lymphoid tumors in mice from the same androgen.

Implants of testes in the spleen of rats resulted in lydig-cell tumors (51). Muhlbock (41, 42) published two papers on the formation of mammary tumors in mice following intraperitoneal injections of the sperm of mice.

Pituitary Hormones

Moon and associates (35, 38, 39, 40) have studied the development of neoplasms in rats treated with pituitary growth hormone. In the first paper they reported the formation of lymphosarcomas of the lung by intraperitoneal injections. In a second paper they noted that neoplastic cells displaced and invaded the adrenal cortex, and in a third paper they reported tumors in the ovaries of rats. The fourth release of the series described the formation of adenomatous lesions of the anterior pituitary.

Smith et al. (48) produced increased growth of transplanted mammary adenosarcoma in mice by subcutaneous injections of pituitary growth hormone.

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SELECTED ABSTRACTS

Effect on the Mammary Tumor Agent on Species Other Than the Mouse. Ambrus, C. M., and Harrisson, J. W. E. *Experientia 8*, 469 (1952). A virus containing extract of homogenized spontaneous mammary tumors obtained from C_3H mice was injected intraperitoneally into young guinea pigs, rats, rabbits, hamsters, C_3H_t mice and deer mice.

The mammary tumor appeared in the C_3H_t mice but did not occur in the other animals during the observation period. When C_3H_t mice (thus free from virus) were suckeled on rats which were previously infected with the tumor extract, they failed to develop tumors indicating that the virus did not appear in rat milk, or was destroyed in the rat's tissues.

Infections in Diabetics Controlled With Terramycin. Walker, Joan B. *The Lancet 1*:521 (1953). Because of the reduced peripheral circulation and reduced resistance to infection, crippling infections in diabetic patients are a constant hazard. In a series of 70 patients treated by the author with oral terramycin, crippling infections were averted in the majority of cases. The need for amputation was reduced, pain was relieved, and a wide variety of organisms were eliminated from ulcers of the hands, feet, respiratory tract, and urinary tract.

The majority of infections in diabetics occur in the feet. Terramycin produced excellent results in 46 of 50 patients with infections of the lower extremities. Swelling and pain subsided within 48 hours. Of these patients 43 were over 60 years of age and all but one were over 50 years of age.

The development of resistance of the organisms to terramycin was not observed by the author, even though several of the patients received several courses of therapy with the antibiotic. This is very important, for with diabetic patients infections are apt to occur again and again.

Toxicity appeared to be quite low. Vomiting and diarrhea was uncommon. This is also important for diabetic patients because vomiting or diarrhea would tend to upset the dietetic control or, at least, require a change in diet. The ease of oral administration is an advantage of this antibiotic.

Effect of the Reticulo-Endothelial Blockade by Thorotrast on the Development of Normal Heterohemagglutinins in Fowl. J. L. Ambrus, C. M. Ambrus, and J. W. E. Harrisson. *Experientia, 7,* 382 (1951). The effect of reticulo-endothelial blockade by Thorotrast on the development of normal rabbit-heterohemagglutinins in the serum of white leghorn chicks was studied. Blood was obtained from the chicks by heart puncture one day after hatching, and thereafter weekly during 9 weeks. Agglutination was studied using microagglutination techniques with rabbit red cells.

It appeared that the maximum quantity of Thorotrast which may be given without lethal effect has no significant effect on normal heterohemagglutin development. Since Thorotrast interferes with antibody production after antigenic stimuli, the results may indicate that normal heterohemagglutinins are produced by an intrinsic maturation process rather than under the effect of external antigens.

The Effect of Isoniazid on Tuberculous Lesions of the Kidneys. Dick, J. C., *The Lancet 1*:808 (1953). Kidneys were obtained by nephrectomy from 9 patients with tuberculosis of the kidneys who had been treated with isoniazid alone for periods of less than one month to three months. The changes in the tuberculous lesions as compared with controls previously obtained from untreated patients were described by the author along with the possible implications as regards the treatment of tuberculosis in general.

The rapid subjective improvement and the regular fall in temperature indicated that isoniazid had a direct action against the tubercle bacilli. There was evidence of absorption of the caseation characteristically present around tuberculous lesions. In chronic lesions this effect was noticed after about 1 month of treatment. Complete absorption of lesions is the aim of treatment, therefore, this effect of isoniazid places it in an important position in therapy.

Untreated tuberculous lesions are characterized by a lack of blood vessels within the lesion, apparently caused by a direct action of the tubercle bacilli on the blood vessels. Following isoniazid therapy the lesions showed an increased vascularity along the edges. No such increase has been found after streptomycin and PAS therapy. In-

creased vascularity provides the mechanism for absorption of the caseation and the homogenized material from old fibrosis. However, the author pointed out some of the possible dangers from such an effect, namely, if the organisms become resistant to isoniazid increased vascularization may expose surrounding tissue to infection with a local extension of the lesion with possible secondary effects resulting from more tissue involvement, and there is also the danger of blood stream dissemination to other parts of the body.

Epitheloid cells play an important part in natural defense against tuberculosis by building a wall or barrier around and through the lesion and by being very closely associated with the development of fibrosis. Streptomycin and PAS both intensify this effect but isoniazid apparently liquidates the epitheloid cells.

Other studies as well as some findings in this report would indicate that some organisms develop resistance to isoniazid. The author suggested that isoniazid alone should not be used for a period of longer than 6 weeks. Other studies have shown that the development of resistance can be reduced by combining with streptomycin therapy. Combined therapy would, therefore, appear to be advisable but the combined effect on histological changes may be entirely different from that found with each drug alone.

BOOK REVIEW

The Official Preparations of Pharmacy. By C. O. Lee, Professor of Pharmacy, Purdue University School of Pharmacy. Second Edition, 544 pages incl. index. The C. V. Mosby Company, St. Louis, 1953. Price $5.50.

In this text, consisting of twenty-five chapters, Dr. Lee systematically considers the definition, description and manufacture of the official pharmaceutical preparations. The second edition of this work has been revised to conform to the *United States Pharmacopeia,* Fourteenth Revision, and the *National Formulary,* Ninth Edition.

The sections dealing with ampuls, tablets and capsules have been rewritten, especially the definitions and descriptions. The trade names of many preparations and a brief statement of the chief action of the preparations have been added to the tabulated information. Cerates, no longer official, have been omitted and Pellets, official for the first time, have been added.

Dr. Lee's text is highly recommended for students beginning the study of pharmaceutical preparations. His fine comments on the phenomena involved in the manufacture of these preparations serves as a substantial aid for the student in his thorough understanding of the official preparations.

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*Kuhn, H. S.: Tr. Am. Acad. Ophth., p. 432, (March-April) 1951.

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